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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,078	07/13/2006	William Alexander Denny	445020	7585

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EXAMINER	
SHIAO, REI TSANG	
ART UNIT	**PAPER NUMBER**
1626	

MAIL DATE	DELIVERY MODE
10/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/577,078	DENNY ET AL.	
	Examiner	Art Unit	
	REI-TSANG SHIAO	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *22 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53 and 57* is/are pending in the application.

4a) Of the above claim(s) *27-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26,51-53 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/05/07,4/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application claims benefit of the foreign application:

NEW ZEALAND 529249 with a filing date 10/31/2003; and

NEW ZEALAND 535618 with a filing date 09/28/2004.

2. Claims 1-53 and 57 are pending in the application.

Information Disclosure Statement

3. Applicant's Information Disclosure Statements filed on January 05, 2007, and April 25, 2006 have been considered. Please refer to Applicant's copies of the 1449's submitted herein.

Responses to Election/Restriction

4. Applicant's election of election of Group I claims 1-26, 51-53 and 57, in the reply filed on July 22, 2008 is acknowledged. Election of a compound of claim 52, i.e., 2-[(2-Bromoethyl)-2,4-dinitro-6-[[[2-phosphonooxy)ethyl]amino]-carbonyl]anilino]ethyl methanesulfonate, as the single species is also acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-53 and 57 are pending in the application. The scope of the invention of the elected subject matter is as follows.

Claims 1-26, 51-53 and 57 are drawn to compounds of formula (I), and their processes of making and methods of use.

Claims 1-26, 51-53 and 57 are prosecuted in the case. Claims 27-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using compounds of formula (I) for treating cells *in vitro*, it does not reasonably provide enablement for using compounds of the formula (I) for treating cancer (i.e., anticancer treatment), *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are:

1. the nature of the invention,

2. the state of the prior art,

3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention of claims 8-21 is drawn to compositions with intent methods of use using compounds of formula (I) for treating cells *in vitro* or *in vivo*.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833,166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the

more specific enablement is necessary in order to satisfy the statute. Koya et al. US 6,743,919, disclose compounds for treating cancer cells in an animal model, see columns 50-51. Applicants are claiming compositions with intent methods of use using compounds of formula (I) effective to "anticancer treatment" *in vivo*. As such, the specification fails to enable the skilled artisan to use the compounds of claims 8-21 effective to "anticancer treatment" *in vivo*.

In addition, there is no established correlation between *in vitro* activity and accomplishing treatment of "anticancer treatment", *in vivo*, and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and those skilled in the ad would not be able to use the compounds of the formula (I) since there is no description of an actual method wherein "anticancer treatment" *in vivo* in a host is treated.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the compounds of claims 8-21 due to the unpredictability of the "treating cancer" *in vivo*. The "anticancer treatment" *in vivo* is known to have many obstacles that would prevent one of ordinary skill in the art from accepting treating or preventing regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the listing of

exemplary in vitro invasion assays of cells, *in vitro*, see pages 58-64 of the specification. There are no *in vivo* working examples present for the treatment cancer ameliorated by the administration of compounds of the instant invention.

The breadth of the claims

The breadth of the claims is compositions with intent methods of use of the instant compounds effective to "anticancer treatment" *in vivo*.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what "anticancer treatment" *in vivo* would be benefited (i.e., treated) by the administration of the instant compounds of the instant invention and would furthermore then have to determine which of the claimed methods of use would provide treatment of cancer *in vivo*, if any.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which methods of use exhibit the desired pharmacological activity and which diseases would benefit from this activity. Thus, the specification fails to provide sufficient support of the broad use of the pharmaceutical compounds of the instant claims 8-21 for the "anticancer treatment" *in vivo*. As a result necessitating one of skill to

perform an exhaustive search for which “anticancer treatment” *in vivo*, can be treated by what pharmaceutical compounds of the instant claims in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that “ a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation, with no assurance of success. This rejection can be overcome by incorporation of the limitation of treating condition (i.e., *in vitro*) would obviate the rejection.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23-26 provide for the use of a transitional metal complex but, since the claim does not set forth any steps involved in the method/process, it is unclear what

method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 23-26 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with37 CFR 3.73(b).

Claims 1-26, 51-53 and 57 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 24 of Patterson et al. co-pending application No.11/654,698. Although the conflicting claims are not identical, they are not patentably distinct from each other and reasons are as follows.

Applicants claim compounds/composition of formula (I), and their methods of use.

Patterson et al. '698 claim method of use using a compound 2-[(2-Bromoethyl)-2,4-dinitro-6-[[[2-phosphonooxy)ethyl]amino]-carbonyl]anilino]ethyl methanesulfonate.

The difference between instant claims and Patterson et al. '698 is that the instant invention claim compounds of formula (I), while Patterson et al. '698 represents a species of the instant claims. The invention of Patterson et al. '698 inherently overlaps with the instant invention.

One having ordinary skill in the art would find the claims 1-26, 51-53 and 57 prima facie obvious because one would be motivated to employ the compound or its method of use of Patterson et al. '698 , to obtain instant compounds of formula (I) and their method of use or processes or making. Dependent claims 2-26, 51-53 and 57 are also rejected along with claim 1 under the obviousness-type double patenting.

The motivation to make the claimed processes derived from the known compound and its method of use of Patterson et al. '698 would possess similar activity (i.e., compositions) to that which is claimed in the reference.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

8. Claims 1, 22 and 53 are objected to because of the following informalities: the term 'including" for the variable R of formula (I) or for composition. Replacement of the term 'including" with a term "selected from" for claim 1, and with a term "comprising" for claims 22 and 53 respectively would obviate the objection.

9. Claims 6 and 7, drawn to product-by-process claims, are objected to for being substantial duplicates of the claims (i.e., claim 1 or 2) from which they depend. When two claims in an application are duplicates, or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to reject the other as being a substantial duplicate of the allowed claim. M.P.E.P. 706.03(k).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rei-tsang Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/REI-TSANG SHIAO /

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October 02, 2008